

## **REMARKS**

Applicants respectfully submit that no prohibited new matter has been introduced by the foregoing amendments. Claims 60-74, 88-92, and 94-110 are pending before the Examiner for examination. Claims 60, 70, 72, 88, 98, 106, and 108 have been amended. Claim 93 has been canceled. Claims 70, 72 106, and 108 have been amended to correct typographic errors. Support for the amended claims can be found throughout the specification and in the original claims. In particular, support for the amendments to claims 60 and 98 can be found at page 32, paragraph 137 and original claim 60. Support for the amendment to claim 88 can be found at page 18, paragraph 78.

The Final Office Action dated August 17, 2004 has been carefully reviewed and the following reply is made in response thereto. In view of the amendments and following remarks, Applicants respectfully submit that the amendments have addressed all the concerns of the Examiner and the claims are now in condition for allowance.

### **Summary of Final Office Action**

1. Claims 60-74 and 88-110 remain rejected under 35 U.S.C. § 112, first paragraph, as based on a disclosure which is allegedly not enabling.
2. Claims 60-74 and 88-110 remain rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter regarded as the invention.
3. Claims 60-74 and 88-110 remain rejected under 35 U.S.C. § 101 because the claimed invention is purportedly directed to non-statutory algorithm type subject matter.
4. Claims 60-92 remained rejected under 35 U.S.C. § 103(a) as purportedly unpatentable over Friend *et al.* (US 6,218,122) taken with Cunningham *et al.* (US 6,372,431).

### **Information Disclosure Statement**

The Examiner indicates that reference number 51 has not been considered because the publication date is not available and the reference is not present in the instant application or its parent. In response, a copy of said reference is submitted concurrently herewith as well as an IDS having the publication date of the reference. Applicants respectfully request that the Examiner initial the Form PTO-1449 and return a copy for Applicants' files.

**The Rejection under 35 U.S.C. § 112, First Paragraph**

Claims 60-74 and 88-110 have been rejected under 35 U.S.C. 112, first paragraph for new matter. The Examiner asserts that the limitation of "a liver cell or tissue sample" in claims 60 and 98 has not been found in the specification. The Examiner's attention is respectfully directed to page 18, paragraph 78 of the specification which discloses that the "cells exposed to the agent are derived from liver tissue." The Examiner is also respectfully directed to Example 1.

Likewise, claims 95-97 have been rejected for allegedly lack of support for the limitations of "at least 10 genes", "at least 50 genes", and "at least 100 genes" of tables 3A-DD. Applicants respectfully direct the Examiner's attention to paragraphs 70 and 99 of the specification. In particular, the specification teaches at paragraph 70 that assays may include the measurement of the expression levels of about 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 50, 75, 100 or more genes from Tables 1-3 and teaches at paragraph 99 that the probe arrays (for use in the claim methods, *etc.*) may contain oligonucleotides that are complementary or hybridize to "at least 2, 3,4, 5, 6, 7, 8, 9, 10, 20, 30, 50, 70, 100 or more genes." It further states that, "[p]referred arrays contain all or nearly all of the genes listed in Tables 1-3 or individually, the gene sets of Tables 3A-3DD."

Because the terms pointed out by the Examiner all have support in the specification, Applicants respectfully submit that the amendments in the previous response have not introduced any new matter. Reconsideration and withdrawal of the rejection are requested.

**The Rejection under 35 U.S.C. § 112, Second Paragraph**

Claims 88-92 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. In particular, the Examiner asserts that claim 88 is unclear as to whether the method is directed to a generic type of cell or tissue, or a specific liver cell or tissue. In response, Applicants have amended claim 88 to recite "a liver cell or tissue." As discussed above, support for the term can be found at page 18, paragraph 78 of the specification. Applicants respectfully request the rejection be withdrawn in view of the amendment.

**The Rejection under 35 U.S.C. § 101**

Claims 60-74 and 93-110 remain rejected under 35 U.S.C. 101 because allegedly the claimed invention is directed to non-statutory algorithm type subject matter. The Examiner asserts that Applicants' previous amendments have not overcome the rejection because the invention still comprises algorithmic steps without any physical alteration resulting from the analytic steps. Without conceding the correctness of the rejection, Applicants have amended claims 60 and 98 to recite a user interface for displaying or providing the results of the data comparison. Support for the amendment can be found at page 32, paragraph 137. The user interface recited in claims 60 and 98 allows a user to interact with a computer system to display or provide the results performed by the software of the computer. The user interface clearly involves a step of element that causes physical transformation of the data outside the computer system or readable medium. Claims 60 and 98 and their dependent claims, as amended, thus do not recite merely an algorithmic step but a post computer-process step outside the computer system and are thus statutory (See MPEP 2106(IV)(B)(2)(b)(i)). Applicants respectfully request that these rejections under 35 U.S.C. §101 be withdrawn in view of the amendments.

**The Rejection under 35 U.S.C. § 103(a)**

Claims 60-74, 88-94, and 98-110 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Friend *et al.* (US 6,218,122 B1, hereafter "Friend") taken with Cunningham *et al.* (US 6,372,431 B1, hereafter "Cunningham"). The Examiner has maintained the rejection on the basis that Applicants' claims do not recite any limitations such as "guidance for developing the database, or the computer system containing the database" and thus the disclosure of Friend of the database comprising expression level of specific gene transcripts of cells exposed to a drug "is consistent with the limitation of database and computer system of the instant claimed invention. (Office Action, page 7, paragraph 30)."

Solely in an effort to expedite prosecution, claims 60 and 98 have been amended to recite that the database comprises information that compares the quantitative gene expression profile from a liver cell or tissue sample exposed to a hepatotoxin and the computer system

comprises a user interface that displays the results of said comparison. Applicants respectfully submit that Friend does not teach or suggest these limitations in addition to the limitations pointed out by Applicants in the previous response.

In addition to the distinctions between Friend and Applicants' invention pointed out in the previous response, Applicants respectfully submit that Friend's invention is directed to methods for analyzing levels of disease states and therapeutic efficacy. The invention purportedly provides physicians a means to monitor changes in organ functions such as in the kidney, liver or heart in response to therapeutic drugs. As stated throughout the reference, Friend *et al.* looks to compare cell perturbation profiles in response to drug therapies. Consistent with the methods disclosed by Friend, the computer system and the databases of the reference serve the same purpose, *i.e.*, perturbation response profiles of diseases or therapies, in particular drug therapies (see col. 19, lines 43-45). Nowhere is there any teaching in the reference of toxins, let alone hepatotoxins. Therefore, contrary to the Examiner's assertion that method and system of Friend *et al.* is directed to a plurality of toxins (paragraph 36 of the Office Action), no hepatotoxins are taught in column 12. In fact the paragraph in column 12, lines 20-25 only discusses therapeutic drugs A, B, and C.

In contrast, Applicants' claimed invention is directed to computer systems, methods of use and computer readable mediums, all of which are related to methods of assessing the toxic impact of a compound on a cell or living organism (page 1 of the specification). While Friend's databases focus on the perturbation response profiles of diseases in response to drug therapies, Applicants' invention is related to the tools used to predict whether a test toxin is a hepatotoxin. Accordingly, Friend does not suggest a computer system containing a database of liver cell or tissue gene expression levels from toxin-exposed and control excipient-exposed samples that can be used to predict a toxic effect of a test agent or hepatotoxicity resulting from exposure to a test agent. Nor does it disclose comparing gene expression levels obtained from a liver cell or tissue sample exposed to a hepatotoxin and control excipient-exposed samples, or a profile of control samples, to predict a toxic effect resulting from exposure to a test agent.

While the Examiner acknowledges that Friend does not teach ANIT and an external database, the Examiner maintains that the deficiencies of Friend are cured by Cunningham. Applicants respectfully submit that Cunningham does not cure the deficiencies of Friend.

Cunningham discloses a method for detecting the effect of a test compound associated with increased or decreased levels of gene expression. However, nowhere does Cunningham teach the use of a database, or a computer system containing a database of quantitative gene expression information for toxin-exposed and control excipient-exposed liver cell or tissue samples that can be used to predict a toxic effect of a test compound or hepatotoxicity resulting from exposure to a test compound as is claimed. Applicants respectfully submit that one of ordinary skill in the art would not have been motivated to modify Cunningham to arrive at the claimed invention.

### **Conclusion**

Applicant respectfully requests reconsideration of the subject application in view of the amendments to the claims and the above remarks. It is respectfully submitted that this application is now in condition for allowance. Should the Examiner feel that there are any issues outstanding after consideration of this amendment, the Examiner is requested to contact the Applicant's undersigned representative.

If there are any fees due in connection with the filing of this amendment, please charge the fees to our Deposit Account No. 50-310. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Dated: **November 17, 2004**

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Respectfully submitted,  
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